

Relationships Among CDISC Variables Concerning Day and Date (CDISC Variable Relationships Part 2 of 3)

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ABSTRACT

This paper explores the relationships among the set of timing variables in CDISC domains. Many CDISC variables are related to each other and understanding relationships among variables helps both in programming and in edit checking. It is hoped that a discussion of relationships among variables, in the context of examples, will help people that are new to CDISC. This paper is one of a short series of example-focused papers devoted to exploring relationships among classes of CDISC variables.

Timing variables are the set of variables that record “time related” characteristics associated with when an event happens. Examples of time-related characteristics are: the visit when the event happened, the date that an event happened, the duration of the event, the number of days between a time point (subject entering the study, etc.), and the date of the event.

All information in this paper is contained in the CDISC Implementation Guide (IG), but it is hoped that a focused discussion of these variables might be of use to the community.

INTRODUCTION

Examples in this paper will be developed from an imaginary study. The study involves a drug that can be administered, via skin-contact patch or a tablet and is part of a regimen that includes moderate exercise (playing in a volleyball league).

Figure 1 is shown in landscape form in an appendix to this paper. For ease of reading, it is suggested that a reader print the figures at the end of the paper and refer to them as the paper is read. The red box in Figure 1 contains cells showing the values of many of the timing variables in the study. It is hoped that this graphic will make the relationships clearer.

Our Study

A peek ahead

Start with the end in mind

A study of a drug that, combined with exercise, helps people lose weight.

Trial Overview																				
Great Valley Volleyball League: Exercise And Weightloss Study																				
All data are fictitious																				
Epochs are recorded on two whole days and two evening sessions in Trial XXX (see pg 104/105) This drug significantly enhances the effects of exercise on losing weight. It takes a long time to effect.																				
Epoch	of clinical encounter or VISIT			Trial Screen	Randomize	Game1	Lab1	Trial Game2	Trial Lab2	Trial Baseline2	Trial Game3	Trial Lab3	Trial Game4	Trial Lab4	Trial PSFU					
Visitnum -> Clinical Encounter Number				1	2	3	4	5	6	7	8	9	10	11	12					
ACCTDY Study DAY ->				-9	-7	1	1	2	0	0	9	15	22	22	29	29	29	36	37	
ARM: Patch-Tab	Element ->			Screen	Baseline & Randomize	Tab & Game	Lab	Tab & Game	Lab	Baseline	Tab & Game	Lab	Tab & Game	Lab	PSFU					
Name	subid and interesting situations concerning the subject			08/21/05	09/01/05	09/09/05	09/09/05	09/15/05	09/15/05	09/22/05	09/23/05	09/23/05	09/29/05	10/06/05	10/07/05	10/14/05				
	screen			PatchTab	Game1 measurement	PAH1	Lab1	PatchTab	Game2	PAH2	Lab2	Break and Baseline 2	PatchTab_Game3	PAH3	Lab3	PatchTab_Game4	PAH4	Lab4	PatchTab_PSFU	
Element ->				V0-Screen			V1-Rand_Base	PatchTab_G1	V3-PatchTab_G2			V4-PatchTab_G3			PatchTab_G4	PatchTab_PSFU				
11	Susan Fehrer	8001	4005_SF	Linking Variable	ER visit	Con Med		Patch -> Table	No	a,1		No	a,1			No	a,c,1,3			
12	Aspirin, No PAH, loses wt.																			
13	German 32, quered when Russ falls on her																			
14	German 32, quered when Russ falls on her																			
15	Elm C1Tally	8002	8005_ED	AE				Patch -> Table	No	a,1		No	a,1,5			No	1		No	
16	Irish 29	Aspirin, non PAH		Can't go in PAH																
17	Irish 29	loses wt		Jamie Finger																
18	Juan Carlos	8003	8006_IC	Lab Units range				Patch -> Table	No	1		YES	a,1			No	a,1		Yes	
19	Spanish 34	Aspirin		Con Med																
20	Spanish 34	lab units wrong		AE																
Name of clinical encounter				screen	BaseRand	Game1	Lab1	game2	lab2	Base2	Game3	Lab3	Game4	Lab4	PSFU					
Visitnum -> Clinical Encounter Number				1	2	3	4	5	6	7	8	9	10	11	12					
ARM: Tab Patch				Screen	Baseline & Randomize	Tab & Game	Lab	Tab & Game	Lab	Baseline	Patch & Game	Lab	Patch & Game	Lab	PSFU					
Element ->				V0-Screen	V1-Rand_Base	V2-TabPatch_G1	V3-TabPatch_G2			V4-TabPatch_G3			V5-TabPatch_G4			V6-TabPatch_PSFU				
26	Russ Lavery	8004	8007_RL	Lab test progress	Delayed visit	lab test range		Tablet -> Patch	YES	a,1,7		YES	a,1,7			4	YES	a,1,4,7,9	YES	a,1,9
27	Drake's last month, Aspirin																			
28	Falls on Susan, loses cell																			
29	Cause 58	Falls on Susan, loses cell																		
30	Vijay Bhaskar	8005	2001_VB	Indian				Tablet -> Patch	No	1		2	No	Business Trip		1	YES		YES	
31	Misses game, business trip			Missing test																
32	Indian 27	Misses game, business trip		Missed Treatment																
33	Erren ruin	8006	8008_E1					Tablet -> Patch	YES			No				No		YES		
34	Aspirin																			
35	Turkish 25																			

Figure 1 (Shown larger below for ease of printing)

Timing variables are in all domains and record information and relationships concerning when an event happened. Several characteristics of “when the event happened” are of interest to the researcher and CDISC has created a set of variables that can record almost any timing characteristic and time-related relationship that could be of interest to a researcher.

While timing variables appear in the many domains, two important variables, RFSTDTC and RFENDTC, are only present in the demography domain, DM. RFSTDTC, often the date-time of first treatment, is the point from which study-day is calculated. RFSTDTC and RFENDTC record the date-time when a subject enters and leaves the study and together they define the period of study participation, a time range. In addition to being used to calculate study day values they are used to create -ENSTRF and -ENENRF variables whose values record a relationship between an event and the start and end of the study period. Often the values are of -ENSTRF and -ENENRF are “BEFORE”, “DURING”, or “AFTER”. -ENSTRF and -ENENRF are imprecise time measurements and are used when an exact date was not recorded.

This “BEFORE” / “DURING” / “AFTER” imprecise classification has been expanded in CDISC STDM IG v3.1.2 by the addition of four timing variables. The variables are -STRTPT and -ENRTPT, which define date-time points and -STTPT and -ENTPT which hold the evaluations made relative to these time points.

DEFINING VISITS, ELEMENTS, EPOCHS

The CDISC Implementation Guide (IG) suggests a new and sometimes confusing structure for describing a subject’s progress through a study. Much of the new structure for reporting progress through a study is to conveniently account for the differences between blinded and unblinded trials. In blinded trials, there is a need to describe subject progress without having to, without being *able* to, know what treatment the subject is receiving. In blinded studies, the schedule for both arms, treatment and control, is usually the same, if not, the treatment can be deduced from treatment pattern and the blinding is flawed. Some of the words to be used in describing subject progress through a study were created or given new meaning by CDISC and therefore bear studying. VISIT used to be the common time marker in a study. VISIT now has a new, more detailed, definition and is less important than in the past.

By CDISC definition, a visit is a clinical encounter. VISITs are defined by rules, in the “Trial Visits (TV) Domain”, that describe both the start and end of the visit. Obviously, the time when a subject comes in for, and leaves from, a visit may vary slightly from the rules.

The VISIT variable is a character variable and contains human readable and meaningfully valued text. Because of this character, human readable nature, sorting by the VISIT variable is not guaranteed to order observations in a sequence that is of interest to investigators. To facilitate sorting, CDISC specified a numeric variable, VISITNUM, corresponding to VISIT and is used for sorting.

A visit can be planned or unplanned. For planned visits, the VISITNUM variable has integer values (4, 6, 23, etc.) and unplanned visits are assigned numbers with a decimal component. An unplanned visit (eg., a lab test) that occurred between planned visits 14 and 15 might have VISIT coded as “Unplanned Lab” and VISITNUM coded as 14.1 in the LB (Laboratory) Domain. What is entered into VISIT, the character-value, human-readable variable describing the clinical encounter, can be fairly free form, especially for unplanned visits. It is suggested that the sponsor attempt to establish logical standards for valuing VISIT and to apply these standards company-wide.

ROLLING UP VISITS

A visit is an encounter between the subject and a person in the study staff, at a point in time. The encounter can be a treatment, a lab test, or a measurement. The exact characteristics of (and rules for) a visit are set in the protocol. This means that subjects will spend most of their time in a state best described as between visits, or “NOT in a visit”. Consider that in our imaginary weight loss study, the administering of the drug takes only a few seconds. The volleyball game that follows drug administration takes two hours. The lab tests, scheduled for the day after the game, take 10 minutes. As a result, a subject spends the great majority of his/her time not interacting with or encountering medical personnel and is “not in visits” most of the time. This makes the description of a subject’s progress awkward and produces sentences like “the subject is between Visit 4 and Visit 5”.

CDISC has created a concept, and variable, called an “ELEMENT” to further describe subject progress. An ELEMENT is defined by two characteristics: 1) a period of time AND 2) what is happening to the subject at that time. An example of an element might be “first lab –scheduled for 9 Sept”. ELEMENTs are *not* visits and can have different start and end points from visits. However, by CDISC definition, one element starts as another begins and subjects are *always* in an element. Since a subject is always in an element, the description of subject progress is made easier if one can use elements to describe progress.

There is freedom in defining the ELEMENT variable associated with a study. ELEMENTs and VISITs need not have the same start and end points. To make things very confusing, not only do the start and end points of visits and

elements not have to align, a visit does not have to be contained in one element. A visit can start in one element and end in another, if the investigator so defines.

Even worse than the confusion over element and visit timing, is the fact that in blinded studies elements cannot be used **at all** to describe subject progress. To know an element one must know two characteristics: the time period and the action taken. With blinded studies, it is usually impossible to know what is happening to the subject (treatment is blinded) during the treatment encounters. Without knowing the treatment being applied to the subject, one cannot know a subject's element at any point in time. Elements are associated with an arm and are of little use in blinded studies.

This inability to assign subjects to elements caused CDISC to create yet another way to describe a subject's progress, the EPOCH variable. An epoch is easy to confuse with an element but is a little less specific, than is an element, on what is happening to the subject. An epoch is similar to an element but is a characteristic of the trial as a whole (not of an arm) and therefore particularly useful in describing blinded studies.

A value for element might be: "Treatment # One - Drug B". Another value for element might be: "Treatment # Three - Drug A". EPOCH values for the same period might be "Trial Treatment One" and "Trial Treatment Three". The epoch simply says that the subject is getting his first treatment or her third treatment. The EPOCH variable does not specify what those treatments are. We see that elements are specific to a study arm and epochs are not tied to a study arm. Because the timing of elements and epochs usually coincide, elements and epochs are easy to confuse. Accordingly, CDISC suggests that EPOCH variables be named or valued with phrases starting with the word "Trial". A value for an ELEMENT might be "Lab 1" and the corresponding value of EPOCH might be "Trial Lab 1".

CDISC has decided that the sponsor should be very explicit in defining visits, elements, and epochs and that the information defining these terms should be included in very structured form in the submission. It was thought that the FDA reviewers and software developers would benefit from having the definitions in called Data Definition Document or DEFINE.XLS.

The order of the Data Definition Document worksheets (the group of Data Definition Document worksheets or tables) have been changed in the CDISC IG v3.1.2. The Subject Visit (SV) and Subject Elements (SE) tables were part of the Trial Design grouping of data in previous CDISC versions and are now considered to be part of the Special Purpose group of tables, with the Demography Domain.

Visits are defined in the Trial Visit table, shown in Figure 2. The investigator specifies "rules" for the start and end of the visit.

Elements are defined in the Trial Element table, shown in Figure 3. The investigator has specified start and end "rules" that are relative to previous study events and not relative to a study day. This has allowed the investigator to specify only "Lab and Game" and "Patch and Game" as values of ELEMENT, rather than "Patch and Game 1" and "Patch and Game 2".

Elements are used to define the "Study Arms" in a table called the "Trial Arms (TA) Table" shown in Figure 4 which includes the "Trial Arms" graphic, showing the use of elements and providing the opportunity to show a timing variable (TAEORD) that is not included in any other table. TAEORD is used to order the elements in the Trial Arm (TA) Table.

An **arm** is a planned sequence of elements. (what happens to a subject)

An **arm** is typically thought of as a treatment group

	A	B	C	D	E	F	G	H	I	J
1	Variable Name	STUDYID	DOMAIN	VISITNUM	VISIT	VISITDY	ARMCD	ARM	TVSTRL	TVENRL
2	Variable Label	Study Identifier	Domain Abbreviation	Visit Sequence Number	Visit Name	Planned Study Day of Visit	Arm Code (Treatment Code)	Description of Arm	Visit Start Rule	Visit End Rule
3	Type	Char	Char	Num	Char	Num	Char	Char	Char	Char
4	Controlled Terms or Format		**TV							
5	Origin	CRF	Derived	CRF or Deived	CRF or Deived	CRF or Deived	Derived	Blank	Blank	Sponsor Defined / Protocol
6	Role	Identifier	Identifier	Identifier	Topic	Timing	Record Qualifier	Synonym Qualifier	Rule	Rule
7	Core	Req	Req	Req	Req	Perm	Exp	Perm	Perm	Perm
8	Note pages 19, 28, 90, 113						8 char max		Rule describing when the Visit starts (Should start, not does start p 113). In relation to the sequence of Elements. Used only when Visits are dependent on occurrences within the study, not fixed by protocol.	Rule describing when the Visits ends, in relation to the sequence of Elements. Visit end rules may be expressed in terms of the start or end of an element, or relative to the start of the visit (
9		GV_VB_WL_4	TV	1	Screen	-8	PatchTab	Patch then Tab	Start of element	1 hour post arrival
10		GV_VB_WL_4	TV	2	BASELINE & RANDOMIZE	-7	PatchTab	Patch then Tab	30 min pre end of Prev. elem.	1 hour post arrival
11		GV_VB_WL_4	TV	3	TAB AND GAME	1	PatchTab	Patch then Tab	1 week after start of prev elem	2.5 hour post arrival
12		GV_VB_WL_4	TV	4	LAB	2	PatchTab	Patch then Tab	1 day post start of Prev element	1 hour post arrival
13		GV_VB_WL_4	TV	5	TAB AND GAME	8	PatchTab	Patch then Tab	6 day post start of Prev element	2.5 hour post arrival
14		S=GV_VB_WL_4	TV	6	LAB	9	PatchTab	Patch then Tab	1 day post start of Prev element	1 hour post arrival
15		GV_VB_WL_4	TV	7	BASELINE2	15	PatchTab	Patch then Tab	6 day post start of Prev element	1 hour post arrival
16		GV_VB_WL_4	TV	8	PATCH & GAME	22	PatchTab	Patch then Tab	1 day post start of Prev element	2.5 hour post arrival
17		GV_VB_WL_4	TV	9	LAB	23	PatchTab	Patch then Tab	1 day post start of Prev element	1 hour post arrival
18		GV_VB_WL_4	TV	10	PATCH & GAME	29	PatchTab	Patch then Tab	6 day post start of Prev element	2.5 hour post arrival
19		GV_VB_WL_4	TV	11	LAB	30	PatchTab	Patch then Tab	1 day post start of Prev element	1 hour post arrival
20		GV_VB_WL_4	TV	12	PSFU	37	PatchTab	Patch then Tab	6 day post start of Prev element	1 hour post arrival
21		GV_VB_WL_4	TV	1	Screen	-8	TabPatch	Tab then Patch	Start of element	1 hour post arrival
22		GV_VB_WL_4	TV	2	BASELINE & RANDOMIZE	-7	TabPatch	Tab then Patch	30 min pre end of Prev. elem.	1 hour post arrival
23		GV_VB_WL_4	TV	3	PATCH & GAME	1	TabPatch	Tab then Patch	1 week after start of prev elem	2.5 hour post arrival
24		GV_VB_WL_4	TV	4	LAB	2	TabPatch	Tab then Patch	1 day post start of Prev element	1 hour post arrival
25		GV_VB_WL_4	TV	5	PATCH & GAME	8	TabPatch	Tab then Patch	6 day post start of Prev element	2.5 hour post arrival
26		S=GV_VB_WL_4	TV	6	LAB	9	TabPatch	Tab then Patch	1 day post start of Prev element	1 hour post arrival
27		GV_VB_WL_4	TV	7	BASELINE2	15	TabPatch	Tab then Patch	6 day post start of Prev element	1 hour post arrival
28		GV_VB_WL_4	TV	8	TAB AND GAME	22	TabPatch	Tab then Patch	1 day post start of Prev element	2.5 hour post arrival
29		GV_VB_WL_4	TV	9	LAB	23	TabPatch	Tab then Patch	1 day post start of Prev element	1 hour post arrival
30		GV_VB_WL_4	TV	10	TAB AND GAME	29	TabPatch	Tab then Patch	6 day post start of Prev element	2.5 hour post arrival
31		GV_VB_WL_4	TV	11	LAB	30	TabPatch	Tab then Patch	1 day post start of Prev element	1 hour post arrival
32		GV_VB_WL_4	TV	12	PSFU	37	TabPatch	Tab then Patch	6 day post start of Prev element	1 hour post arrival

Figure 2

	B	C	D	E	F	G
1	STUDYID	DOMAIN	ETCD	ELEMENT	TESTRL	TEENRL
2	Study Identifier	Domain Abbreviation	Element Code	Description of Element	Rule for Start of Element	Rule For End of Element
3	Char	Char	Char	Char	Char	Char
4		**TE				
5	CRF	Derived	Sponsor Defined	Sponsor Defined or Protocol	Sponsor Defined or Protocol	Sponsor Defined or Protocol
6	Identifier	Identifier	Record Qualifier	TOPIC	Rule	Rule
7	Req	Req	Req	Req	Req	Perm
8			8 Char Max Abbrev			
9			8 char name of ELEMENT. Used in transposing	TOPIC Variable for Element-- the name of the element	Expressed rule for beginning the element	Expressed rule for ending the element
10	GV_VB_WL_4	TE	SCRN	Informed consent and screen	Inf Consent	Taking Baseline measurements
11	GV_VB_WL_4	TE	B1R	Baseline 1: measurements & Randomization	Day After Inf Consent	First Dose (tab or patch)
12	GV_VB_WL_4	TE	PTGM	Apply Patch - play game	Application of Patch	Lab test in Morning
13	GV_VB_WL_4	TE	TBGM	Take Tablet - play game	Swallowing of Tab	Lab test in Morning
14	GV_VB_WL_4	TE	LAB	Lab tests	Day after game	Next Dose (tab or patch)
15	GV_VB_WL_4	TE	B2	Baseline2: measurements	Measurement - 6 days after game2	Next Dose (tab or patch)
16	GV_VB_WL_4	TE	PSFU	PSFU	Arrival at P.I. Office	Leaving P.I. Office
17						

There are no breaks between elements.

The end of an element is the start of the next element.

An **element** is the basic building block of time (but not the smallest) and has:

A definition of the start of the element. The start of an element is usually the start of treatment.

A rule for ending the element. This is often the planned duration of the element.

Figure 3

An **arm** is a planned sequence of elements. (what happens to a subject)

An **arm** is typically thought of as a treatment group

	B	C	D	E	F	G	H	I	J	K	L
1	STUDVID	DOMAIN	ARMCD	ARM	TAETORD	ETCD	ELEMENT	TABRANCH	TATRANS	EPOCH	
2	Study Identifier	Domain Abbreviation	Arm Code (Treatment Code)	Arm Description of Arm (Treatment Group)	TAETORD Order of Element within Arm	Element Code	Description of Element	Branch	Transition Rule	Trial Epoch	
3	Char	Char	Char	Char	Num	Char	Char	Char	Char	Char	
4		TA									
5	CRF	Derived	Derived	Derived	Sponsor Defined	Sponsor Defined	Sponsor Defined or Protocol	Blank	Blank	Blank	
6	Identifier	Identifier	Topic	Synonym Qualifier	Identifier	Record Qualifier	Synonym Qualifier	Rule	Rule	Rule	
7	Req	Req	Req	Req	Perm	Perm	Perm	Exp	Exp	Perm	
8			If char max abbr for ARM. Used for transposing. If timing of visits for a trial does not depend on arm then ARMCD should be null					Condition subject met at a "branch" in the trial design at the end of this element. (e.g. randomized to Drug A)			
9	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	1	SCRN	Screen			TRIAL SCREEN	
10	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	2	B1R	BASELINE & RANDOMIZE	assign 2 Tab-Patch		TRIAL BASELINE RANDOMIZE	
11	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	3	TBGM	TAB AND GAME		if injured, go to element 12	TRIAL GAME1	
12	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	4	LAB	LAB			TRIAL LAB1	
13	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	5	TBGM	TAB AND GAME		if injured, go to element 12	TRIAL GAME2	
14	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	6	LAB	LAB			TRIAL LAB2	
15	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	7	B2	BASELINE2			TRIAL BASELINE2	
16	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	8	PTGM	PATCH & GAME		if injured, go to element 12	TRIAL GAME3	
17	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	9	LAB	LAB			TRIAL LAB3	
18	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	10	PTGM	PATCH & GAME		if injured, go to element 12	TRIAL GAME4	
19	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	11	LAB	LAB			TRIAL LAB4	
20	GV_VB_WL_4	TA	TABPATCH	TAB-PATCH	12	PSFU	PSFU			TRIAL PSFU	
21	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	1	SCRN	SCREEN			TRIAL SCREEN	
22	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	2	B1R	BASELINE & RANDOMIZE	assign 2 Patch-Tab		TRIAL BASELINE RANDOMIZE	
23	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	3	PTGM	PATCH & GAME		if injured, go to element 12	TRIAL GAME1	
24	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	4	LAB	LAB			TRIAL LAB1	
25	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	5	PTGM	PATCH & GAME		if injured, go to element 12	TRIAL GAME2	
26	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	6	LAB	LAB			TRIAL LAB2	
27	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	7	R2	RASFI INF?			TRIAL RASFI INF?	
28	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	8	TBGM	TAB AND GAME		if injured, go to element 12	TRIAL GAME3	
29	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	9	LAB	LAB			TRIAL LAB3	
30	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	10	TBGM	TAB AND GAME		if injured, go to element 12	TRIAL GAME4	
31	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	11	LAD	LAD			TRIAL LAD4	
32	GV_VB_WL_4	TA	PATCHTAB	PATCH-TAB	12	PSFU	PSFU			TRIAL PSFU	
33											

Figure 4

The relationship between values of the EPOCH and ELEMENT variables can be seen in Figure 4.

The above "Trial Design (TD)" tables define how a study should be conducted. As we know it is a rare study in which all subjects follow the protocol exactly. A submission should also contain tables that describe the actual progress of subjects through a study. These tables are: Protocol Violations (PV), Subject Elements (SE), and Subject Visits (SV). A description of these tables is beyond the scope of this paper.

The time and date of events are recorded in the ISO 8601 format. This format can record times and duration at any desired level of precision. For a paper on the subject, please refer to "ISO 8601 – An International Standard for Date and Time Formats" by Shi Tao Yeh. It should be noted that the CDISC IG v3.1.2 has an expanded section that discusses the ISO 8601 standard.

We will only discuss ISO 8601 to a depth that allows us to understand the examples we will give. Figure 5 gives some examples of dates and durations in ISO 8601 format.

Information is recorded from left to right-- from large units of time to small. Unknown values in the middle of a value cannot be left blank, but unknown values on the far right hand side of the string may be left blank. Dates are recorded as a four digit year, then a dash, then a two digit, zero filled month, another dash, followed by a two digit, zero filled day.

If there is information on time to be recorded, a "T" is used to separate the date information from the time information. To the right of the "T" is a two digit zero filled hour that records 24-hour clock time, followed by a colon, then a two digit zero filled minute, followed by another colon, and a two zero filled digit second. Decimal seconds may also be recorded.

The separator between date units is a dash and between the time units is a colon.

Dates and Durations as ISO 8601

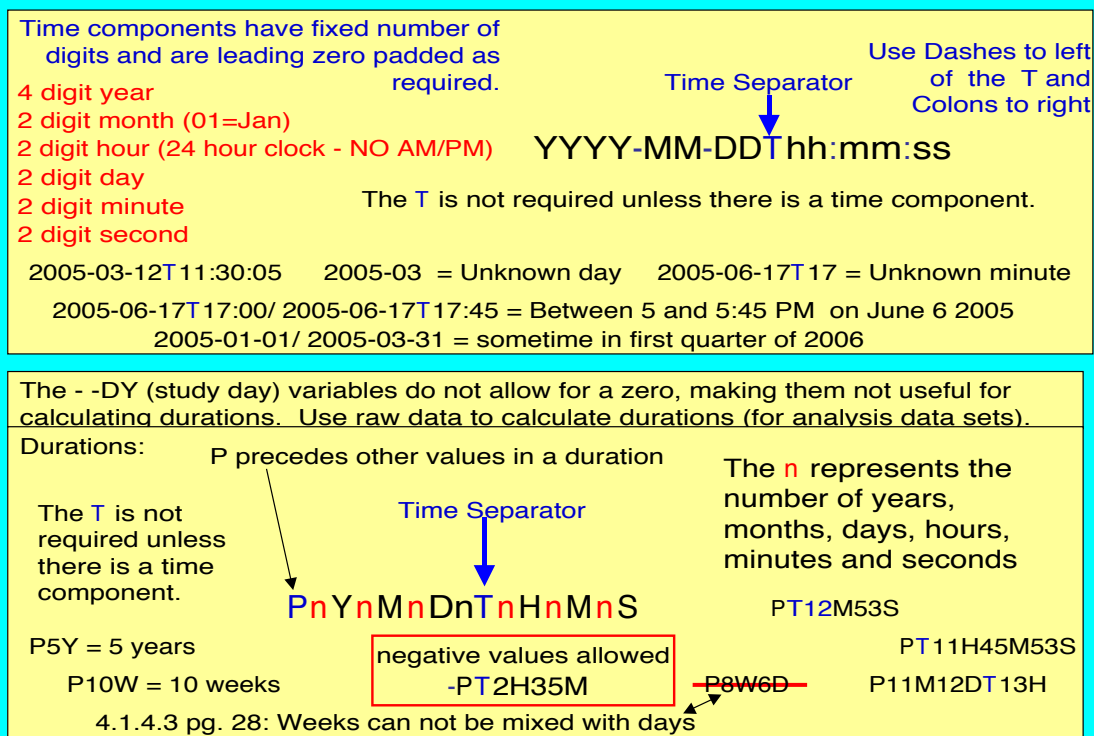


Figure 5

Figure 6 shows the relationship among some of the timing variables. We say that the information in Figure 6 is free-standing because it does not “tie in with” the data for the weight loss study shown in other figures. Also, it shows only a few of the timing variables. While these are flaws in the example, it allows us to show some of the timing variables in larger fonts as well as discuss the meaning and some special characteristics of the variables.

VISIT is character and is in human readable form. Visit names are defined in the protocol and should agree with the values in the trial tables. VISITNUM is numeric and allows for easy sorting of observations. Unplanned visits have fractional values in VISITNUM and values describing the occurrence in VISIT. VISITDY is the planned day of the visit and has values for planned visits but not for unplanned visits. Susan was called back to have tests repeated, causing an unplanned visit. LBDTC is the actual date-time of the visit in ISO 8601 format. LBDY is the actual “study day of the event” or the number of days since RFSTDTC in DM. In a well managed study, most of the visits will happen on the planned day. Unlike VISITDY, which is the planned day of the visit and can have missing values if the event is unplanned, LBDY is the actual day of the event and should always be valued.

In addition to being used to calculate study day values, RFSTDTC and RFENDTC are used to populate two variables: -STRF and -ENRF. These variables record whether an event occurred before, during, or after the subject was in the study. This before, during, and after study participation classification has been expanded in CDISC SDTM IG v3.1.2. Two timing variables, -STRTPT and -ENRTPT, define new time points and the evaluation, before, during, concurrent, and after, are recorded in two variables, -STTPT and -ENTPT. These four variables have been added to allow the creation of new time points and the relating of data elements to these new points. These variables are not shown in any graphic.

VISIT, VISITDY, VISITNUM (Interventions, Events, & Findings)

VISITNUM: Clinical encounter Number. Numeric Version of VISIT, used for sorting. Expected for LB, EG, VS as timing variable. Can be collected on CRF or derived.

- -DTC: **Actual** Visit date-time in character format (ISO 8601).

- -DY: **Actual** Study Day of laboratory collection, measured as integer days relative to RFSTDTC in Demographics

Example from Laboratory Domain

USUBJID	VISIT	VISITNUM	(Planned) VISITDY	(Actual Date) LBDTC	(Actual) LBDY
4005-SF	Screen1	1	-8	2005-08-31	-8
4005-SF	Screen2	1.1		2005-09-02	-6
4005-SF	lab1	4	2	2005-09-09	2
4005-SF	lab2	6	9	2005-09-16	9

VISIT : Protocol defined description (name) of clinical encounter Permissible in LB . May be recorded on CRF or Derived.

VisitDY: **Planned** Study Day of VISIT. Relative to RFSTDTC in DEMOGRAPHICS)

the - -DY variables use a formula that does not return a zero

Figure 6

To support the final example and figure, we offer the following situation in the study. This example explores recording values for repeated events in the study described above. To collect an additional set of data points, the investigator asked two people to submit to additional lab tests. The investigator wanted a measure of how the stress of the volleyball game was reflected in lab tests and was able to persuade two players to be tested before, at half time and immediately after the end of the game. Results for one game (the first game played) are shown in the figure below.

The subjects were Susan and Russ.

- -ELTM, - -ENDTC, - -TPT, - -TPTNUM, - -TPTREF (Interventions & Findings)

Example from Labs Domain where we measure a value before, during and after the first volleyball game. The game runs from 6PM (1800 hours) to 8PM(2000 hours).

Measure at 5PM (1700 hours), 7 PM (1900 hours) & 8PM (2000 hours).

		Clin. Encounter					
		Actual Study Day	Planned Study Day			Start of Specimen Collection	End of Specimen Collection
USUBJID	VISIT	LBDY	VISIT NUM	VISIT DY	LBSTDTC	LBSTDC	LBENDTC
4005_SF	GLab1	1	3	1	2005-09-08T17	2005-09-08	2005-09-08T17:05
4005_SF	GLab1	1	3	1	2005-09-08T19	2005-09-08	2005-09-08T19:05
4005_SF	GLab1	1	3	1	2005-09-08T20	2005-09-08	2005-09-08T20:05
8007_RL	GLab1	1	3	1	2005-09-08T17:05	2005-09-08	2005-09-08T17:10
8007_RL	GLab1	1	3	1	2005-09-08T19:05	2005-09-08	2005-09-08T19:10
8007_RL	GLab1	1	3	1	2005-09-08T20:06	2005-09-08	2005-09-08T20:11

Character Sequencer	Numeric Sequencer	Reference Point	Elapsed Time	Optional Reference ID	Start rel. to Study	End rel. to Study	Duration	Result
LB	LB	LB	LB	LB	LB	LB	LB	LB
TPT	TPTNUM	TPTREF	ELTM	REFID	STRF	ENRF	DUR	ORRES
PreGame	1	GameStart	-PT1H	Null	Null	Null	Null	9.1
MidGame	2	GameStart	PT1H	Null	Null	Null	Null	6.3
PostGame	3	GameStart	PT2H	Null	Null	Null	Null	5.1
PreGame	1	GameStart	-PT55M	Null	Null	Null	Null	7.1
MidGame	2	GameStart	PT1H5M	Null	Null	Null	Null	7.0
PostGame	3	GameStart	PT2H5M	Null	Null	Null	Null	6.8

Figure 7

The visit was named Glab1 (G for Game– Lab1 for lab test collected during game 1). Since the VISIT had been defined as the whole experience of being dosed and playing the volleyball game, VISITNUM is valued as 3 for all three records. VISITDY is the same as the day of the first game. The Reference point for the - -DY calculation is the day of first dose. First dosing happens just before the first game, so this VISITDY has a value of 1 (zero is not allowed in any - -DY variables). LBSTDTC and LBENDTC record the start and end of dosing. LBSTDC is the day of the test and should have a value when LBSTDTC and LBENDTC have values.

LBPTPT is used to further identify the times for repeated events. LBPTPT has human readable values and LBPTPTNUM has numeric values that allow for easy sorting. Values of LBPTPTNUM are allowed to repeat for different subjects as both Susan and Russ have values LBPTPTNUM values =1.

LBPTPTREF contains a value that is the reference point for elapsed time calculations. In this case we are recording the time of the test in reference to the start of the game. Since the first test happens before the start of the game, it has a negative elapsed time in LBELTM and a negative elapsed time is allowed by ISO 8601. The LBREFID could be used to establish a relationship between this observation and some external data source but is null in this case. It could be deleted from the data set, because it is not a required variable and is shown only to facilitate our discussion in the paper. LBSTRF and LBENRF should be null, or not included, because the actual start and end of the events were recorded in LBSTDTC and LBENDTC. LBDUR is null, because it is only has a value if it is recorded on the CRF. We offer as support of the fact LBDUR is not collected, the fact that LBSTDTC and LBENDTC are valued to allow duration to be calculated programmatically if needed for analysis data sets. The authors suggest that collecting start, end, and duration information will not improve the accuracy of the data, but will cause data validation errors when there is a difference between the recorded - -DUR value and the calculated duration value.

SUMMARY

The timing variables in CDISC domains are both complex and interrelated. It is hoped that this treatment of these variables, as a group, is of use to the community.

REFERENCES

Yeh, Shi-Tao, "ISO 8601 – An International Standard for Date and Time Formats", Proceedings of NESUG 2006 Conference, Coders Corner Paper 17, <http://www.nesug.org/proceedings/nesug06/cc/cc17.pdf>

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Our Study

A peek ahead

Start with the end in mind
A study of a drug that, combined with exercise, helps people lose weight.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T							
1		Trial Overview																		Great Valley Volleyball League: Exercise And Weightloss Study				All data are fictitious			
2	ISO 8601 date format is YYYY-MM-DD. This drug magically enhances the effect of exercise on losing weight. It has a long term effect.																										
3	Epoch	Epochs are features of the whole trial and the naming convention is Trial XXX (see pg 106/159)			Trial Screen	Trial Randomize	Trial Game1		Trial Lab1	Trial Game2		Trial Lab2		Trial Baseline2		Trial Game 3		Trial Lab3	Trial Game 4	Trial Lab4	Trial PSFU						
4	Name of clinical encounter or VISIT				screen	BaseRand	Game1		lab1	game2		lab2		Base2		Game3		lab3	Game4	Lab4	PSFU						
5	Visitnum --> Clinical Encounter Number				1	2	3		4	5		6		7		8		9	10	11	12						
6	AESTDY	Study DAY -->			-8	-7	1	1	2	8		8		9		15	22	22	23	29	29	30	37				
7		ARM= Patch-Tab			Element -->	Screen	Baseline & Randomize	Patch & Game		Lab	Patch & Game		Lab		Baseline		Tab & Game		Lab	Tab & Game		Lab	PSFU				
8		subjid and interesting situations concerning the subject			08/31/05	09/01/05 and take baseline measurement	09/08/05	09/08/05	09/09/05	09/15/05		09/15/05		09/16/05		09/22/05	09/29/05	09/29/05	09/30/05	10/06/05	10/06/05	10/07/05	10/14/05				
9		Name			screen	baseline measurement	PatchTab_Game1	PAH1	Lab1	PatchTab_Game2		PAH2		Lab2		Break and Baseline 2	PatchTab_Game3	PAH3	Lab3	PatchTab_Game4	PAH4	Lab4	PSFU				
10	Element -->				W0-Screen	W1-Rand_Base	PatchTab_G1	W3 - PatchTab_G2								W4 - PatchTab_G3				PatchTab_G4		PatchTab_PSFU					
11	Susan Fehrer 1001 4005_SF				Linking Variable	Patch -> Tablet	No		a, 1	No		a, 1						No		a, c, 1, 3	No						
12	Aspirin, No PAH, loses wt.				ER visit																						
13	German 32 injured when Russ falls on her				Con Med																						
14	Erin O'Mally 1002 8005_ED				AE	Patch -> Tablet	No		a, 1	No		a, 1, 5						1		No							
15	Aspirin, no PAH				Can't go to PAH																						
16	Irish 29 loses wt				Jams Finger																						
17	Juan Carlos 1003 8006_JC				Lab Units range	Patch -> Tablet	No		1	YES		a, 1						No		a, 1	Yes						
18	Aspirin				Con Med																						
19	Spanish 34 lab units wrong				AEs																						
20																											
21																											
22	Name of clinical encounter				screen	BaseRand	Game1		lab1	game2		lab2		Base2		Game3		lab3	Game4		Lab4	PSFU					
23	Visitnum --> Clinical Encounter Number				1	2	3		4	5		6		7		8		9	10		11	12					
24		ARM= Tab- Patch			Element -->	Screen	Baseline & Randomize	Tab & Game		Lab	Tab & Game		Lab		Baseline		Patch & Game		Lab	Patch & Game		Lab	PSFU				
25		Element -->			W0-Screen	W1-Rand_Base	W2-TabPatch_G1	W3 - TabPatch_G2								W4 - TabPatch_G3				W5-TabPatch_G4		W6-TabPatch_PSFU					
26	Russ Lavery 1004 8007_RL				Lab test progress	Tablet -> Patch	YES		a, 1, 7	YES		a, 1, 7						4	YES	a, 1, 4, 7, 9	YES		a, 1, 9				
27	Drinks too much, Aspirin				Delayed test																						
28	Cauc 58 Falls on Susan, injures self				lab test range																						
29	Vijay Bhaskar 1005 2001_VB				Indian	Tablet -> Patch	No		1	2		No		Business Trip		1	YES			YES							
30	Misses game, business trip				Missing test																						
31	Indian 27				Missed Treatment																						
32	Ersen Tulin 1006 8008_ET					Tablet -> Patch	YES		No								No						YES				
33	Aspirin																										
34																											
35	Turkish 35																										